REMARKS

Status of the Claims

Claims 39, 43, 45-48, and 52-70 are currently pending. Claims 39, 43, 45-48, and 52-70 have been amended. The amendments do not represent new matter. Claims 40-42, 44, 49, and 71-76 have been canceled. In addition, claims 1-38 and 50-51 have been previously canceled.

Interview Summary

The undersigned wishes to thank the Examiner Saidha for the opportunity to discuss this case on January 17, 2006, in order to address outstanding rejections in the present application. In particular, the claimed invention was discussed in light of the Koizumi reference (Koizumi et al., 1998, *Nature Biotechnology* 16: 847-850). Also discussed were the enablement and the written description requirements as they apply to the invention.

The amendments contained in this paper are substantially as suggested by the Examiner. Claim 39 has been amended to narrow the types of cells used to practice the invention to *E. coli* LacZ$^-$ and to yeast cells. Claim 39 and claims dependent therefrom have also been amended to recite an "isolated cell," in accordance with the Examiner's assertion that this would clarify that the invention is directed toward bioengineered cells.

The Rejections Under 35 U.S.C. § 112

Claims 39-48 and 52-70 were rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 39-48 and 52-70 were further rejected under 35 U.S.C. § 112, as containing subject matter which was not described in the specification as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. For brevity's sake, the remarks in response to these two types of rejection have been combined, because the evidence necessary to support both requirements is similar.

The Office Action asserts that none of the pending claims are enabled by the specification. The rejection states that the scope of the claims is not commensurate with the enablement provided by the disclosure. Applicants respectfully disagree. Using the specification as a guide, one of ordinary skill in the art could make and use a prokaryotic or a yeast cell that produces a glycoconjugate of interest in the absence of an exogenously supplied nucleotide without undue experimentation, wherein the prokaryotic or a yeast cell comprises heterologous genes encoding one or more sugar nucleotide regenerating enzyme and one or more glycosyltransferase.

Genes encoding enzymes involved in sugar-nucleotide generation and regeneration were known in the art at the time of filing (page 10, lines 14-16). In addition to this high level of skill in the art, the specification provides examples of combinations of enzymes that may be used to regenerate many sugar nucleotides including UDP-Gal (page 11, lines 3-9, and FIGS. 1, 3, 4, 5, and 15), UDP-Glc (page 11, lines 11-26, and FIGS. 6 and 18), UDP-GlcNAc (page 12, lines 5-26, and FIG. 7), UDP-GalNAc (page 13, line 2, to page 14, line12, and FIG. 8), UDP-GlcA (page 14, line 14, to page 15, line14, and FIGS. 6, 9, and 19), CMP-NeuNAc (page 15, line 16, to page 17, line 4, and FIG. 10), GDP-Man (page 17, line 6, to page 18, line 4, and FIG. 12), GDP-Fuc (page 18, line 6, to page 20, line 19, and FIGS. 12 and 17).

As indicated in the specification (page 21, lines 13-18), glycosyltransferases and their properties were well known in the art at the time of filing. The specification provides specific an extensive list of examples of glycosyltransferases that may be used based on their donor specificity (page 22, line 8, to page 26, line 4). The specification further provides for the recombinant expression of eukaryotic enzymes in prokaryotes (e.g., expression of a human UDP-GlcA transferase in *E. coli*; page 37, lines 22-23; expression of various mammalian enzymes for glycoconjugate synthesis in cells such as *E. coli*, namalwa cells, COS cells; page 30, line 23, to page 31, line 26). Given this teaching and the level of understanding of recombinant expression in the art, one of skill in the art could express an enzyme having a particular glycosyltransferase activity in an organism without undue experimentation.

Although glycosyltransferases may lack high degree of sequence homology among different families, they do, however, share sequence identities and similarities

among members in the same family. Furthermore, their crystal structures fall into only two categories: glycosyltransferases-A (GT-A, or GT-A like) and glycosyltransferases-B (GT-B) families (Ha *et al.*, 2000, *Protein Science* 9: 1045-1052; Hu and Walker, 2002, *Chemical Biology* 9:1287-1296; Vrielink *et al.*, 1994, *EMBO Journal* 13: 3413-3422; Gibson et al., 2002, *J. Chemical Biology* 9: 1337-1346; Bourne and Henrissat, 2001, *Current Opinion in Structural Biology* 11: 593-600).

One of skill in the art may recognize that certain eukaryotic glycosyltransferases may not be efficiently expressed in prokaryote cells and vice versa. As the specification describes on page 29, line 10, to page 30, line 22, other expression systems, including yeast, insect cells, or animal cells, may be used instead. Because often there are eukaryotic and prokaryotic enzymes known in the art that have the same or similar glycosyltransferase activity, if one wished to use a prokaryotic expression system, one of skill in the art could choose to use the prokaryotic enzyme having the desired activity.

The specification provides several working examples of "superbugs." The examples describe the construction and use of three different superbugs, not just one. Moreover, the enzymes used to produce the superbugs were not all of *E. coli* origin

Furthermore, in the examples shown in the patent application [a host cell transformed with a nucleic acid encoding sugar-nucleotide regenerating enzymes viz., (1) galactokinase (GalK), (2) galactose-l-phosphate uridylyltransferase (GalT), (3) glucose-1-phosphate uridylyltransferase (GalU), and (4) pyruvate kinase (PykF), and a glycosyltransferase, viz. (5) αl,3-galactosyltransferase (from bovine) for the production of oligosaccharides (e.g. α-galactose)], the αl,3-galactosyltransferase used was cloned from bovine; it was not from *E. coli*. The superbug of Example 2 contained an αl,4GalT gene from *Neisseria meningitidis*, gram-negative diplococcus (page 57, lines 5-15). The superbug of Example 3 contained a sucrose synthase gene from *Anabaena sp.*, a cyanobacterium (page 62, lines 8-10), and an αl,3-galactosyltransferase from bovine.

The examples provide assays that can be used to test for the ability of the organism to recombinantly express a functional enzyme and to test for the ability of the enzymes to work together to produce the desired product, prior to constructing the superbug. One of skill in the art could screen for appropriate enzymes and combination of enzymes that function together in a certain system prior to going through the process

of putting all the genes for the enzymes together to create a superbug. Thus, using the specification as a guide, the amount of experimentation needed by one of skill in the art to make and use the claimed invention would not be undue.

As further evidence that the invention can be realized as described in the specification, Applicants submitted on June 23, 2005 an Appendix A containing post-filing publications by one or more of the co-inventors describing the use of the methods for creation of different prokaryotic and eukaryotic superbugs producing: αES in *E. coli* (Chen *et al.*, 2001, *J. Am. Chem. Soc.* 123: 8866-8867); αKTUF in *E. coli* (Chen *et al.*, 2002, *ChemBioChem* 3: 47-53); CKTUF in *E. coli* (Zhang *et al.*, 2003, *Org. Biomolecular Chem.* 1: 3048-3053); and SEα in yeast (Shao *et al.*, 2003, *Appl. Environ. Microbiol.* 69: 5238-5242).

As discussed above, the specification is replete with examples of enzymes having given activities, enzymes that may be used together to regenerate sugar nucleotides, and figures providing diagrams of plasmids that are useful in creating the cells of the present claims, along with descriptions as how to create the plasmids. The sequences of thousands of sugar nucleotide regenerating enzymes, epimerases, and glycosyltransferases were known in the art at the time of filing. Moreover, the specification provides several working examples of cells of the present claim. Based on this, a skilled artisan would know how to make and use the claimed invention without undue experimentation. Accordingly, the claims are enabled and the enablement rejection should be withdrawn.

Further, the Federal Circuit recently reiterated that the written description requirement should be deemed satisfied as long as a reasonable artisan of the relevant field, having read the specification, then knows what the invention is. *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005). Here, a skilled artisan would recognize that at the time of filing the Applicants were in possession of a cell that produces a glycoconjugate of interest in the absence of an exogenously supplied nucleotide triphosphate and comprises heterologous genes encoding one or more sugar nucleotide regenerating enzyme and one or more glycosyltransferase. Indeed, multiple examples are provided. Accordingly, the claims satisfy the written description requirement and that rejection should also be withdrawn.

The Rejections Under 35 U.S.C. § 102

Claims 39-42, 50-53, and 62-63 were rejected under 35 U.S.C. § 102(b) as being anticipated by Koizumi *et al.*, 1998, *Nature Biotechnology* 16: 847-850 (Koizumi). Applicants respectfully disagree.

The Koizumi reference describes a production system that includes more than one cell. Koizumi uses a combination of metabolically engineered *E. coli* with a nucleoside-5' triphosphate producing microorganism, *C. ammoniagenes* (see Discussion in Koizumi, p. 849). For example, shown in Figure 1 in Koizumi is a production system of UDP-Gal and globotriose that uses three different types of cells (two types of *E. coli* cells and a *C. ammoniagenes* cell). However, the Koizumi reference does not disclose a single cell that produces a glycoconjugate of interest in the absence of an exogenously supplied nucleotide triphosphate, as called for in amended claim 39. Therefore, not every element of the invention recited in amended claim 39 is described in the Koizumi reference.

Since amended claim 39 now recites patentable subject matter, claims 44, 46-48, and 52-70, which depend therefrom, now set forth additional subject matter further defining Applicants' claimed invention over the cited reference. In view of the above amendments and arguments, Applicants therefore request the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 102(b).

Finally, claim 52 has been amended to recite "sucrose synthase" rather than "sucrose synthetase". No new matter has been added in making the amendment, because both "sucrose synthase" and "sucrose synthetase" are synonyms for the enzyme classified as EC 2.4.1.13. "Sucrose synthase" is the more common name of the enzyme.

Conclusion

In light of the amendments and comments made herein, Applicants submit that the application is in condition of allowance and requests notification thereof. The

Examiner is invited to call the undersigned to discuss any matter that may expedite allowance of this application. The Director is authorized to charge any additional fees or underpayment of fees regarding this response, including extensions for reply, to Deposit Account 23-1925.

Respectfully submitted,

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